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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,384	02/18/2004	David Spencer	HO-P02165US1	2112

26271 7590 12/27/2006
FULBRIGHT & JAWORSKI, LLP
1301 MCKINNEY
SUITE 5100
HOUSTON, TX 77010-3095

EXAMINER	
LI, QIAN JANICE	
ART UNIT	PAPER NUMBER
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/27/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/781,384	SPENCER ET AL.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed 10/6/2006 are acknowledged. Claims 1-24 have been canceled; claims 25-53 are pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 10/6/06 response would be addressed to the extent that they apply to current rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The prior rejection of Claims 6-8, 13, 21, 23, 24 under 35 U.S.C. 102(a) as being anticipated by *Dicker et al* (WO 02/36769), is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The prior rejection of Claims 1-4, 6-9, 11, 13-18, 20-23 under 35 U.S.C. 103(a) as being unpatentable over *Dicker* (WO 02/36769), in view of *Nair et al* (USP 6,670,186), is withdrawn, in view of the amendment.

The prior rejection of Claim 19 under 35 U.S.C. 103(a) as being unpatentable over *Dicker* (WO 02/36769), in view of *Nair et al* (USP 6,670,186) as applied to claims 1-4, 6-9, 11, 13-18, 20-23 above, further in view of *Shu* (US 2003/0082163), is withdrawn, in view of the amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of Claims 1-24 now applies to claims 25-53 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for activating an antigen-presenting cell comprising transfecting an antigen presenting cell

ex vivo with an expression vector, or *in vivo* in a subject by gene gun-mediated intradermal route, wherein the expression vector comprises a polynucleotide encoding a chimeric protein comprising a myristoylation membrane targeting region, a FK506-binding protein region, a CD40 cytoplasmic polypeptide region lacking the CD40 extracelluar domain, operably linked to a promoter; does not reasonably provide enablement for activating an antigen-presenting cell comprising transfecting an antigen presenting cell *in vivo* with said expression vector by any route of administration; does not reasonably provide enablement for activating APCs with said vector, wherein the vector encodes any ligand-binding region, for reasons of record and following.

Applicants argue that the specification provides multiple working examples in support of the claimed subject matter.

In response, it is noted the rejection is a scope one. The matter at issue is that the instant disclosure does not support the full scope of the claims. The paragraphs 0217 to 0218 of the specification describe a nucleic acid comprising the coding sequence for FKBP12 binding domain, the myristoylation-targeting domain, and CD40 cytoplasmic region, but not the genus of the ligand-binding region. The paragraphs 0225 to 0232 of the specification describe *ex vivo* activation of APCs, not *in vivo*. The paragraphs 0236 to 0238 of the specification describe biolistic delivery of said nucleic acid construct, not any other route of effective delivery. The paragraphs 0243 to 024 of the specification describe making a transgenic mouse whose genome incorporated iCD40, wherein the levels of iCD40 expression varied from barely detectable to easily

detectable in the PCR-positive offsprings, and it is unclear whether these mice could be used for pharmaceutical purpose was unclear at the time of instant filing.

The paragraphs 0082 to 0095 of the specification generally name several non-protein drug-ligand binding pairs, such as cyclophilin receptors, the steroid receptors, and tet receptor. However, it fails to teach that these systems are suitable for inducing CD40 receptor dimerization, and it fails to teach how these systems would function when placed together with any membrane targeting region, and the CD40 cytoplasmic polypeptide in the context of chemically induced dimerization for manipulating signal transduction. Turning to the state of the art, at the time of instant priority date, few CID systems were available (*Kopytek et al*, Chem & Biol 2000;7:313-21), and the FKBP system was one of the original CID systems, and still under development. *Amara et al* (PNAS 1997;94:10618-23) teach, "OWING TO THE COMPLEXITY OF THESE COMPOUNDS, ADJUSTING THEIR BINDING OR PHARMACOLOGICAL PROPERTIES BY CHEMICAL MODIFICATION IS DIFFICULT" (e.g. the abstract). Thus, it is evident that at the time of the invention, the skilled in the art, while acknowledging the significant potential of chemically induced dimerization for modulating signal transduction pathways in various cells, still recognized that such usage was neither routine nor accepted, and awaited significant development and guidance for its practice. Therefore, it is incumbent upon applicants to provide sufficient and enabling teachings within the specification for such therapeutic regimen. Although the instant specification provides a list of systems that may be used as non-protein drug binding pairs, it is not enabled for its full scope because the

specification fails to provide an enabling disclosure for the functional characteristics of the genus.

In conclusion, beyond the FK506-binding protein, the specification fails to teach which other ligand-binding region could be used in the re-engineered CD40 receptor that provides potent pharmacological activation of APCs. The specification fails to teach direct *in vivo* administration of said vectors beyond gene gun-mediated intradermal administration would transfect sufficient numbers of DCs to assert a pharmaceutical effect, and thus fails to provide an enabling disclosure.

Therefore, in view of the limited guidance, the lack of predictability of the art, and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is **571-272-0730**. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is **(866) 217-9197**. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has

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For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL
December 20, 2006